

### **Remarks**

Claims 1 and 3-13 are pending. Claims 1 and 12 have been amended. Importantly, the claim amendments should not be construed to be an acquiescence to any of the claim rejections. Rather, the amendments are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to prosecute further the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

### **Claim Rejections under 35 USC § 103(a)**

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the references relied upon by the Examiner; or they must be among the variations that would have been “obvious to try” to one of ordinary skill in the relevant art in light of the cited references. Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the combination of cited references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

#### **US 2006/0140984 in view of US 5,143,717, in further view of WO 96/03115**

The Examiner contends that claims 1 and 3-13 are unpatentable over US 2006/0140984 in view of US 5,143,717, in further view of WO 96/03115. The Applicants respectfully traverse.

The Applicants respectfully contend that the Examiner has failed to state a *prima facie* case of obviousness because the cited combination of references fails to teach or suggest all of the limitations of the rejected claims.

For reasons stated in an earlier Response, US 2006/0140984 does not qualify as prior art under 35 USC § 102(e) against the instant application with respect to “hydrofluoroalkane propellants” because that feature is not disclosed in the underlying provisional application. Further, US 2006/0140984 lacks disclosure of the oil phase being a solid or semi-solid at room temperature, as required by current claims 1, 12, 13, and the claims dependent therefrom. It

necessarily follows that US 2006/0140984 also fails to teach the limitation as to the specific range of the solid or semi-solid oil phase in the emulsion.

Further, US 5,143,717 does not teach hydrofluoroalkane propellants. Moreover, US 5,143,717 does not teach the presence of a solid or semi-solid oil phase in the quantity required by amended claims 1, 12, 13, and the claims dependent therefrom.

In other words, the combined teaching of US 2006/0140984 (which is not available to the Examiner with respect to “hydrofluoroalkane propellants”) and US 5,143,717 does not include all of the limitations of the rejected claims because, for example, neither document discloses a hydrofluoroalkane propellant or the requirement for the presence of the solid or semi-solid oil phase in from about 0.5% to about 3.0% by weight of the emulsion.

The Examiner has also advanced WO 96/03115 as part of her rejection of claims 1 and 3-13. However, the disclosure of WO 96/03115 does not overcome the shortcomings of the combination of US 2006/0140984 (which is not available to the Examiner with respect to “hydrofluoroalkane propellants”) and US 5,143,717 with respect to the showing of a *prima facie* case of obviousness because the missing claim limitations would not have been obvious to try to one of skill in the art as of the priority date of the instant application.

WO 96/03115 is directed towards foamable *aqueous* compositions; whereas, the current claims are directed towards oil-in-water emulsions. One of ordinary skill in the art would appreciate the significant differences between aqueous solutions and oil-in-water emulsions, and the ramifications of these differences with respect to formulation processes and the compatibility of components. The cited reference stresses the importance of using a propellant that is a “water-immiscible liquefied gas” (WO 96/03115, page 3, lines 6-7), and teaches that hydrofluoroalkane (HFA) propellants are suitable alternatives to propane, butane, or pentane. One of ordinary skill in the art would have understood that the solubility of 1,1,1,2-tetrafluoroethane in water is 0.15 wt%; as a comparison, the solubility of ethane in water is 4.7 wt%. Moreover, the cited reference teaches that the propellants *must* have a variety of properties in order to be suitable alternative foaming agents, including: immiscibility with water (vehicle), liquefied when pressurized, relatively high boiling point, and relatively low vapor pressure (page 4, lines 21-25). However, the solubility of HFA propellants in an oil-in-water emulsion would arguably be much higher; consequently, an HFA propellant would not meet all of the stated four

requirements of a suitable propellant outlined in the reference. Therefore, one of ordinary skill in the art would not have considered HFA propellants to be among the finite number of suitable alternatives that would have been obvious to try.

In this regard, WO 96/03115 teaches away from the use of a HFA propellant with an oil-in-water emulsion. It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulation of successful foam compositions is an unpredictable process. Given the guidance provided by WO 96/03115, one of ordinary skill in the art attempting to develop a foamable oil-in-water emulsion would have pursued a propellant that was immiscible with the emulsified vehicle.

Furthermore, one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed foamable oil-in-water emulsions given the disclosures of the three cited references. Only WO 96/03115 teaches the use of HFA propellants in formulating foam compositions. However, this reference, as discussed above, teaches four criteria necessary for a propellant to form a successful foam composition. HFA propellants would not have the necessary solubility characteristics described in the reference and, therefore, one of ordinary skill in the art would not have had a reasonable expectation of successfully developing a foam formulation comprising an HFA propellant and an oil-in-water emulsion.

Moreover, in further support of the absence of a *prima facie* showing of obviousness of the rejected claims based on the art cited by the Examiner, the Applicants refer the Examiner to Exhibits A, B, and C. Exhibits A, B, and C are articles describing the challenges associated with replacing CFCs with HFAs in certain pharmaceutical compositions. The Montreal Protocol on Substances That Deplete the Ozone Layer was signed in 1987 and banned CFCs from further use; however, exceptions were made until suitable alternatives were discovered for “essential uses” where the public health benefit of using CFCs outweighed the harm to the environment. Many pharmaceutical compositions described in these articles still contained CFCs as recently as 2001, because *no suitable alternative had been found after 14 years of research*. The resulting

low expectation of success with respect to the use of HFA propellants in formulations that typically comprise CFCs or hydrocarbons, such as those described in the cited references, is well documented. Indeed, the specification as filed outlines the potential challenges associated with substituting HFA propellants for traditional propellants. The chemical and physical properties of HFAs differ significantly from those of alkanes and CFCs; substitution of HFAs for these propellants would require significant experimentation and reformulation, with little expectation of success.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

US 2006/0233721 in view of US 6,075,056, in further view of WO 96/03115

The Examiner contends that claims 1 and 3-13 are unpatentable over US 2006/0233721 in view of US 6,075,056, in further view of WO 96/03115. The Applicants respectfully traverse.

The Applicants contend that the Examiner has failed to state a *prima facie* case of obviousness; the combination of references fails to teach or suggest all of the limitations of the rejected claims.

For reasons stated in an earlier Response, US 2006/0233721 does not qualify as prior art under 35 USC § 102(e) against the instant application with respect to “hydrofluoroalkane propellants” because that feature is not disclosed in the two underlying provisional applications with sufficiently early filing dates. Further, US 2006/0233721 lacks disclosure of the oil phase being a solid or semi-solid at room temperature, as required by current claims 1, 12, 13, and the claims dependent therefrom. It necessarily follows that US 2006/0233721 also fails to teach the limitation as to the specific range of the solid or semi-solid oil phase in the emulsion.

Further, US 6,075,056 does not teach the use of hydrofluoroalkane propellants. The cited reference also fails to teach compositions comprising a solid or semi-solid oil phase in the quantity required by the rejected claims. Indeed the sole formulation disclosed in the reference suitable for use as an aerosol formulation (column 12, line 14) is the aqueous “liquid formulation” described in Table H (column 11). However, this “liquid formulation” does not comprise a solid or semi-solid oil phase. Moreover, the disclosed “liquid formulation” is not an oil-in-water emulsion, as required by the rejected claims.

The Examiner has also advanced WO 96/03115 as part of her rejection of claims 1 and 3-13. However, the disclosure of WO 96/03115 does not overcome the shortcomings of the combination of US 2006/0233721 (which is not available to the Examiner with respect to “hydrofluoroalkane propellants”) and US 6,075,056 with respect to the showing of a *prima facie* case of obviousness because the missing claim limitations would not have been obvious to try to one of skill in the art as of the priority date of the instant application.

The foamable compositions disclosed in both US 6,075,056 and WO 96/03115 are foamable *aqueous* compositions; whereas, the current claims are directed towards oil-in-water emulsions. One of ordinary skill in the art would appreciate the significant differences between aqueous solutions and oil-in-water emulsions, and the ramifications of these differences with respect to formulation processes and the compatibility of components. The cited reference stresses the importance of using a propellant that is a “water-immiscible liquefied gas” (WO 96/03115, page 3, lines 6-7), and teaches that hydrofluoroalkane (HFA) propellants are suitable alternatives to propane, butane, or pentane. One of ordinary skill in the art would have understood that the solubility of 1,1,1,2-tetrafluoroethane in water is 0.15 wt%; as a comparison, the solubility of ethane in water is 4.7 wt%. Moreover, the cited reference teaches that the propellants *must* have a variety of properties in order to be suitable alternative foaming agents, including: immiscibility with water (vehicle), liquefied when pressurized, relatively high boiling point, and relatively low vapor pressure (page 4, lines 21-25). However, the solubility of HFA propellants in an oil-in-water emulsion would arguably be much higher; consequently, an HFA propellant would not meet all of the stated four requirements of a suitable propellant outlined in the reference. Therefore, one of ordinary skill in the art would not have considered HFA propellants to be among the finite number of suitable alternatives that would have been obvious to try.

In this regard, WO 96/03115 teaches away from the use of a HFA propellant with an oil-in-water emulsion. It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulation of successful foam compositions is an unpredictable

process. Given the guidance provided by WO 96/03115, one of ordinary skill in the art attempting to develop a foamable oil-in-water emulsion would have pursued a propellant that was immiscible with the emulsified vehicle.

Furthermore, one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed foamable oil-in-water emulsions given the disclosures of the three cited references. Only WO 96/03115 teaches the use of HFA propellants in formulating foam compositions. However, this reference, as discussed above, teaches four criteria necessary for a propellant to form a successful foam composition. HFA propellants would not have the necessary solubility characteristics described in the reference and, therefore, one of ordinary skill in the art would not have had a reasonable expectation of successfully developing a foam formulation comprising an HFA propellant and an oil-in-water emulsion.

Moreover, in further support of the absence of a *prima facie* showing of obviousness of the rejected claims based on the art cited by the Examiner, the Applicants refer the Examiner to Exhibits A, B, and C. Exhibits A, B, and C are articles describing the challenges associated with replacing CFCs with HFAs in certain pharmaceutical compositions. The Montreal Protocol on Substances That Deplete the Ozone Layer was signed in 1987 and banned CFCs from further use; however, exceptions were made until suitable alternatives were discovered for “essential uses” where the public health benefit of using CFCs outweighed the harm to the environment. Many pharmaceutical compositions described in these articles still contained CFCs as recently as 2001, because *no suitable alternative had been found after 14 years of research*. The resulting low expectation of success with respect to the use of HFA propellants in formulations that typically comprise CFCs or hydrocarbons, such as those described in the cited references, is well documented. Indeed, the specification as filed outlines the potential challenges associated with substituting HFA propellants for traditional propellants. The chemical and physical properties of HFAs differ significantly from those of alkanes and CFCs; substitution of HFAs for these propellants would require significant experimentation and reformulation, with little expectation of success.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

US 4,808,388 in view of US 5,858,331

The Examiner contends that claims 1, 3, 5-9, and 11-13 are unpatentable over US 4,808,388 in view of US 5,858,331. The Applicants respectfully traverse.

The Applicants contend that the Examiner has failed to state a *prima facie* case of obviousness because the combination of references fails to provide the required reasonable expectation of success in developing the claimed inventions.

The compositions disclosed in US 4,808,388 are purely cosmetic in nature; i.e., they contain no therapeutically active ingredients. Whereas, the compositions described in US 5,858,331 are complexes of an active ingredient with a hydrofluoroalkane propellant. However, the compositions of the '331 patent are not oil-in-water emulsions. Indeed, the '331 patent specifically teaches away from the use of water in the compositions because its presence disrupts the association of the active ingredient, "resulting in release of the HFC propellant" (column 3, lines 20-23). In other words, US 5,858,331 teaches away from the use of water in the presence of an active agent. Critically, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. Moreover, one of ordinary skill in the art would have appreciated that the formulation of successful foam compositions is an unpredictable process. Given the guidance provided by US 5,858,331, one of ordinary skill in the art attempting to develop a foamable oil-in-water emulsion comprising an active ingredient would not have pursued use of an HFC propellant. Given the specific instructions in US 5,858,331 to avoid the use of water in the presence of an HFC propellant and an active agent, one of ordinary skill in the art would not have had a reasonable expectation of success in combining the teachings of the two cited references.

Furthermore, rejected claim 1 is limited to a formulation comprising "a propellant consisting essentially of a hydrofluoroalkane or a mixture of hydrofluoroalkanes, without additional co-solvents or co-propellants." Notably, US 4,808,388 implicitly teaches away from the use of an HFA propellant without the use of a co-propellant because the propellant systems disclosed in the '388 patent are limited to nitrous oxide, and various mixtures of nitrous oxide with carbon dioxide, nitrogen, or HFA propellants (column 3, lines 11-14). In other words, the

fact that the '388 patent is silent as to systems without a co-propellant is relevant to an assessment of *prima facie* obviousness because such variations of the propellant system would arguably be "obvious to try" to one of ordinary skill. Given the facts that the '388 patent is the sole cited reference that teaches an oil-in-water emulsion, and it impliedly teaches away from the use of an HFA propellant without the use of a co-propellant, one of ordinary skill would not have had a reasonable expectation of success in the claimed inventions (i.e., using HFA as a propellant without the use of a co-propellant for an oil-in-water system).

Finally, as discussed in the preceding sections, the low expectation of success with respect to the use of HFA propellants in formulations that typically comprise CFCs or hydrocarbons, such as those described in the cited references, is well documented. Indeed, the specification as filed outlines the potential challenges associated with substituting HFA propellants for traditional propellants. The chemical and physical properties of HFAs differ significantly from those of alkanes and CFCs; substitution of HFAs for these propellants would require significant experimentation and reformulation, with little expectation of success.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

US 4,808,388 in view of US 5,858,331, in further view of US 2005/0042182

The Examiner contends that claims 4 and 10 are unpatentable over US 4,808,388 in view of US 5,858,331, as applied to claim 1 above, in further view of US 2005/0042182. The Applicants respectfully traverse.

As outlined above, the Applicants contend that the combination of US 4,808,388 and US 5,858,331 fails to provide a *prima facie* case of obviousness with respect to claims 1 and the claims dependent therefrom. Claims 4 and 10 depend, directly or indirectly, from claim 1. Importantly, the teachings in US 2005/0042182 do not address the shortcomings of US 4,808,388 and US 5,858,331 vis-à-vis claim 1, and therefore with respect to claims 4 and 10.

US 2005/0042182 fails to teach or suggest the use of HFA propellants in topical compositions comprising members of additional classes of active agents. The use of HFA propellants in the claimed formulations, therefore, would have been unobvious to try to one of



ordinary skill in the art at the time of the invention, notwithstanding the additional teachings of US 2005/0042182.

As compared to the combination of US 4,808,388 and US 5,858,331, inclusion of the disclosure of US 2005/0042182 would not provide one of ordinary skill in the art any additional reason to expect success in forming a foamable oil-in-water emulsion encompassed by the rejected claims. HFA propellants are not strict substitutes for traditional propellants. The disclosure of the three cited references supports this assertion. The inventors of US 4,808,388 use HFA propellants only in mixtures with other propellants; the disclosure of US 5,858,331 relates to exploitation of the unique solubility properties of HFA propellants to use the propellant as the solvent for the active agent, as well as for its compressed gas properties; and US 2005/0042182 fails to disclose the use of HFA propellants. As discussed in the preceding sections, the low expectation of success with respect to the use of HFA propellants in formulations that typically comprise CFCs or hydrocarbons, such as those described in the cited references, is well documented. Indeed, the specification as filed outlines the potential challenges associated with substituting HFA propellants for traditional propellants. The chemical and physical properties of HFAs differ significantly from those of alkanes and CFCs; substitution of HFAs for these propellants would require significant experimentation and reformulation, with little expectation of success.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

WO 96/03115 in view of US 5,143,717

The Examiner contends that claims 1, 3-5, and 12-13 are unpatentable over WO 96/03115 in view of US 5,143,717. The Applicants respectfully traverse.

The Applicants respectfully contend that the Examiner has failed to state a *prima facie* case of obviousness because the cited combination of references fails to teach or suggest all of the limitations of the rejected claims. Critically, the Applicants have argued above that the combination of US 2006/0140984, Davis and Sachetto fails to constitute a *prima facie* showing of obvious with respect to the rejected claims; necessarily, therefore, the Applicants respectfully contend that the combination of Sachetto and Davis fails to meet the Examiner's evidentiary burden with respect to the rejected claims.

For example, the combination of the cited references fails to teach each and every limitation of claim 1 because neither reference teaches the exclusion of volatile lower alcohols from the foam formulations. Further, US 5,143,717 does not teach hydrofluoroalkane propellants. Moreover, US 5,143,717 does not teach the presence of a solid or semi-solid oil phase in the quantity required by amended claims 1, 12, 13, and the claims dependent therefrom. In other words, the combined teaching of Sachetto and Davis does not include all of the limitations of the rejected claims because, for example, neither document discloses a hydrofluoroalkane propellant or the requirement for the presence of the solid or semi-solid oil phase in from about 0.5% to about 3.0% by weight of the emulsion.

Moreover, WO 96/03115 is directed towards foamable *aqueous* compositions; whereas, the current claims are directed towards oil-in-water emulsions. One of ordinary skill in the art would appreciate the significant differences between aqueous solutions and oil-in-water emulsions, and the ramifications of these differences with respect to formulation processes and the compatibility of components. The cited reference stresses the importance of using a propellant that is a “water-immiscible liquefied gas” (WO 96/03115, page 3, lines 6-7), and teaches that hydrofluoroalkane (HFA) propellants are suitable alternatives to propane, butane, or pentane. One of ordinary skill in the art would have understood that the solubility of 1,1,1,2-tetrafluoroethane in water is 0.15 wt%; as a comparison, the solubility of ethane in water is 4.7 wt%. Moreover, the cited reference teaches that the propellants *must* have a variety of properties in order to be suitable alternative foaming agents, including: immiscibility with water (vehicle), liquefied when pressurized, relatively high boiling point, and relatively low vapor pressure (page 4, lines 21-25). However, the solubility of HFA propellants in an oil-in-water emulsion would arguably be much higher; consequently, an HFA propellant would not meet all of the stated four requirements of a suitable propellant outlined in the reference. Therefore, one of ordinary skill in the art would not have considered HFA propellants to be among the finite number of suitable alternatives that would have been obvious to try.

In this regard, WO 96/03115 teaches away from the use of a HFA propellant with an oil-in-water emulsion. It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a

direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulation of successful foam compositions is an unpredictable process. Given the guidance provided by WO 96/03115, one of ordinary skill in the art attempting to develop a foamable oil-in-water emulsion would have pursued a propellant that was immiscible with the emulsified vehicle.

Furthermore, one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed foamable oil-in-water emulsions given the disclosures of Sachetto and Davis. Only WO 96/03115 teaches the use of HFA propellants in formulating foam compositions. However, this reference, as discussed above, teaches four criteria necessary for a propellant to form a successful foam composition. HFA propellants would not have the necessary solubility characteristics described in the reference and, therefore, one of ordinary skill in the art would not have had a reasonable expectation of successfully developing a foam formulation comprising an HFA propellant and an oil-in-water emulsion.

Finally, as discussed in the preceding sections, the low expectation of success with respect to the use of HFA propellants in formulations that typically comprise CFCs or hydrocarbons, such as those described in the cited references, is well documented. Indeed, the specification as filed outlines the potential challenges associated with substituting HFA propellants for traditional propellants. The chemical and physical properties of HFAs differ significantly from those of alkanes and CFCs; substitution of HFAs for these propellants would require significant experimentation and reformulation, with little expectation of success.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

### **Fees**

The Applicants believe that no fees are required in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any required fee to our Deposit Account, **06-1448** reference **CPX-015.01**.

### **Conclusion**

In view of the above remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

Respectfully submitted,

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